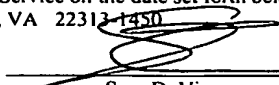
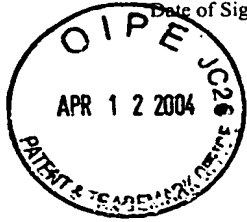


I hereby certify that this correspondence is being deposited with the United States Postal Service on the date set forth below as First Class Mail in an envelope addressed to: Commissioner for Patents, P O Box 1450, Alexandria, VA 22313-1450

Date of Signature and Deposit: April 9, 2004

  
Sara D. Vinarov



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Rui Sousa

Date: April 9, 2004

Serial No.: 10/689,495

Art Unit:

Filed: 10/20/2003

Examiner:

For: METHODS FOR USING DOUBLE-MUTANT  
RNA POLYMERASES WITH REDUCED  
DISCRIMINATION BETWEEN NON-CANONICAL  
AND CANONICAL NUCLEOSIDE TRIPHOSPHATES

Docket: 310307.90240

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
P O Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed is a completed Form PTO-1449 listing documents which the applicant in the above-identified application wishes to bring to the attention of the Examiner for consideration in connection with the examination on the merits of this application.

This application is a continuation-in-part of U.S. Patent Application Serial No 10/404,726, filed April 1, 2003 which claims priority from U.S. Serial No. 09/965,346, filed September 27, 2001, which is a continuation of 09/643,189 filed August 21, 2000, which is a continuation of U.S. Serial No. 09/100,803, (U.S. Patent No. 6,107,037) filed June 19, 1998, which is a divisional of U.S. Serial No. 08/713,331 (U.S. Patent No. 5,849,546), filed September 13, 1996.

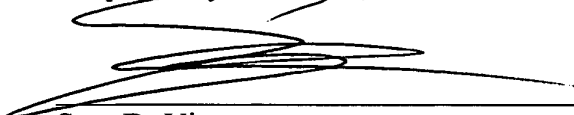
Applicant hereby assert that in each of the above cross-referenced related applications, the requisite Information Disclosure Statements and U.S. PTO 1449 forms were timely filed. Applicant notes that under 37 C.F.R. § 1.98(d), copies of documents that were earlier cited by or submitted to the Office in a prior application that is relied on for an earlier effective filing date do not have to be re-submitted. Accordingly, applicant has enclosed herewith only copies of the Information Disclosure Statements accompanied by the relevant

PTO-1449 forms that were previously submitted to the USPTO, in each of the above-identified cross-reference applications. Copies of the previously cited publications are not included herein.

In addition, applicant has enclosed herewith, a current Form PTO-1449 along with copies of the documents listed therein, which were not previously submitted to the Office.

No fee is believed due in connection with this submission. However, should any fee be due, please charge the fee to Deposit Account No. 17-0055.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read 'Sara D. Vinarov', written over a horizontal line.

Sara D. Vinarov  
Reg. No. 48,524  
Quarles & Brady LLP  
P O Box 2113  
Madison, WI 53701-2113

TEL (608)251-5000  
FAX (608)251-9166



FILED WITH APPLICATION  
NO. 10/404,726

EXPRESS MAIL LABEL NO. EV161876709US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Continuation Of:

Applicants: Rui Sousa, et al.  
Serial No.: 09/965,346  
Filed: September 27, 2001  
For: METHODS FOR USING MUTANT RNA  
POLYMERASES WITH REDUCED  
DISCRIMINATION BETWEEN NON-CANONICAL  
AND CANONICAL NUCLEOSIDE  
TRIPHOSPHATES  
Group Art Unit: 1634  
Examiner: A. Chakrabarti

Commissioner For Patents  
Washington, D.C. 20231

---

INFORMATION DISCLOSURE STATEMENT

---

Dear Sir:

Pursuant to 37 C.F.R. 1.98, enclosed herewith is a list of documents which the Applicants in the above-identified patent application wish to bring to the attention of the Examiner for consideration in connection with the examination on the merits of this patent application.

The documents in this Information Disclosure Statement were cited in application Serial No. 09/965,346, filed on September 27, 2001. Therefore, Applicants have not enclosed an extra copy of these documents.

### U.S. Patents

4,683,195; Mullis, et al.; July 28, 1987.

### Other Documents

"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," Biotechniques 9(2):142-146, 1990.

W.M. Barnes, et al., "DNA Sequencing by Partial Ribosubstitution," J. Mol. Biol. 119:83-99, 1978.

E.T. Butler and M.J. Chamberlin, "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5772-5778, 1982.

C. Cazenave, et al., "RNA Template-directed RNA Synthesis by T7 RNA Polymerase," PNAS 91:6972-6976, 1994.

D.H. Jones and B.H. Howard, "A Rapid Method for Recombination and Site-specific Mutagenesis by Placing Homologous Ends on DNA Using Polymerase Chain Reaction," Biotechniques 10(1):62-66, 1991.

G.A. Kassavetis, et al., "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5779-5788, 1982.

D.A. Kostyuk, et al., "Mutants of T7 RNA Polymerase that are Able to Synthesize Both RNA and DNA," FEBS Letters 369:165-168, 1995.

H. Kotani, et al., "Nucleotide Sequence and Expression of the Cloned Gene of Bacteriophage SP6 RNA Polymerase," Nucl. Acids Res. 15(6):2653-2664, 1987.

R. Sousa and R. Padilla, "A Mutant T7 RNA Polymerase as a DNA Polymerase," EMBO J. 14(18):4609-4621, 1995.

E. Uhlman, et al., "Antisense Oligonucleotides: A New Therapeutic Principle," Chem. Rev. 90:543-593, 1990.

A. Wolfgang, et al., "Kinetic Characterization of Ribonuclease-resistant 2'-modified Hammerhead Ribozymes," Science 253:314-317, 1991.

No fees are believed necessary to enter this Statement. However, if any fees are necessary please charge Deposit Account 17-0055.

Respectfully submitted,

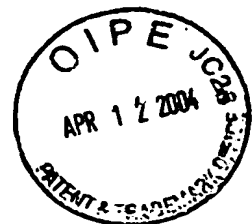
Rui Sousa, et al.

April 1, 2003

By: \_\_\_\_\_  
Jean C. Baker  
Reg. No. 35,433  
Quarles & Brady LLP  
411 East Wisconsin Avenue  
Milwaukee, WI 53202-4497  
(414) 277-5709



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.



PTO/SB/08B (10-01)  
Approved for use through 10/31/2002. OMB 0651-0031  
U. S. Patent and Trademark Office: U. S. DEPARTMENT OF COMMERCE  
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<b>Substitute for form 1449B/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)  Sheet 2 of 2				<b>Complete If Known</b>	
				Application Number	
				Filing Date	
				First Named Inventor	
				Group Art Unit	
				Examiner Name	
				Attorney Docket Number	
				310307.90061	

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," Biotechniques 9(2):142-146, 1990.	
		W.M. Barnes, et al., "DNA Sequencing by Partial Ribosubstitution," J. Mol. Biol. 119:83-99, 1978.	
		E.T. Butler and M.J. Chamberlin, "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5772-5778, 1982.	
		C. Cazenave, et al., "RNA Template-directed RNA Synthesis by T7 RNA Polymerase," PNAS 91:6972-6976, 1994.	
		D.H. Jones and B.H. Howard, "A Rapid Method for Recombination and Site-specific Mutagenesis by Placing Homologous Ends on DNA Using Polymerase Chain Reaction," Biotechniques 10(1):62-66, 1991.	
		G.A. Kassavetis, et al., "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5779-5788, 1982.	
		D.A. Kostyuk, et al., "Mutants of T7 RNA Polymerase that are Able to Synthesize Both RNA and DNA," FEBS Letters 369:165-168, 1995.	
		H. Kotani, et al., "Nucleotide Sequence and Expression of the Cloned Gene of Bacteriophage SP6 RNA Polymerase," Nucl. Acids Res. 15(6):2653-2664, 1987.	
		R. Sousa and R. Padilla, "A Mutant T7 RNA Polymerase as a DNA Polymerase," EMBO J. 14(18):4609-4621, 1995.	
		E. Uhlman, et al., "Antisense Oligonucleotides: A New Therapeutic Principle," Chem. Rev. 90:543-593, 1990.	
		A. Wolfgang, et al., "Kinetic Characterization of Ribonuclease-resistant 2'-modified Hammerhead Ribozymes," Science 253:314-317, 1991.	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



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PTO/SB/17 (10-03)

Approved for use through 07/31/2006. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

# FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$ ) 0.00

**Complete if Known**

Application Number	10/689,495
Filing Date	10/20/2003
First Named Inventor	Rui Sousa
Examiner Name	
Art Unit	
Attorney Docket No.	310307.90240

**METHOD OF PAYMENT (check all that apply)**☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None☒ Deposit Account:Deposit Account Number  
Deposit Account Name

17-0055

Quarles &amp; Brady LLP

The Director is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☒ Credit any overpayments☒ Charge any additional fee(s) or any underpayment of fee(s)☐ Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.**FEE CALCULATION****1. BASIC FILING FEE**

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1001 770	2001 385	Utility filing fee	
1002 340	2002 170	Design filing fee	
1003 530	2003 265	Plant filing fee	
1004 770	2004 385	Reissue filing fee	
1005 160	2005 80	Provisional filing fee	
<b>SUBTOTAL (1)</b>			<b>(\$ ) 0.00</b>

**2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE**

Total Claims	Extra Claims	Fee from below	Fee Paid
Independent Claims	-20* =	X	0.00
Multiple Dependent Claims	-3** =	X	0.00

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description
1202 18	2202 9	Claims in excess of 20
1201 86	2201 43	Independent claims in excess of 3
1203 290	2203 145	Multiple dependent claim, if not paid
1204 86	2204 43	** Reissue independent claims over original patent
1205 18	2205 9	** Reissue claims in excess of 20 and over original patent

**SUBTOTAL (2)** (\$ ) 0.00

\*\*or number previously paid, if greater; For Reissues, see above

**FEE CALCULATION (continued)****3. ADDITIONAL FEES**

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1051 130	2051 65	Surcharge - late filing fee or oath	
1052 50	2052 25	Surcharge - late provisional filing fee or cover sheet	
1053 130	1053 130	Non-English specification	
1812 2,520	1812 2,520	For filing a request for <i>ex parte</i> reexamination	
1804 920*	1804 920*	Requesting publication of SIR prior to Examiner action	
1805 1,840*	1805 1,840*	Requesting publication of SIR after Examiner action	
1251 110	2251 55	Extension for reply within first month	
1252 420	2252 210	Extension for reply within second month	
1253 950	2253 475	Extension for reply within third month	
1254 1,480	2254 740	Extension for reply within fourth month	
1255 2,010	2255 1,005	Extension for reply within fifth month	
1401 330	2401 165	Notice of Appeal	
1402 330	2402 165	Filing a brief in support of an appeal	
1403 290	2403 145	Request for oral hearing	
1451 1,510	1451 1,510	Petition to institute a public use proceeding	
1452 110	2452 55	Petition to revive - unavoidable	
1453 1,330	2453 665	Petition to revive - unintentional	
1501 1,330	2501 665	Utility issue fee (or reissue)	
1502 480	2502 240	Design issue fee	
1503 640	2503 320	Plant issue fee	
1460 130	1460 130	Petitions to the Commissioner	
1807 50	1807 50	Processing fee under 37 CFR 1.17(q)	
1806 180	1806 180	Submission of Information Disclosure Stmt	
8021 40	8021 40	Recording each patent assignment per property (times number of properties)	
1809 770	2809 385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810 770	2810 385	For each additional invention to be examined (37 CFR 1.129(b))	
1801 770	2801 385	Request for Continued Examination (RCE)	
1802 900	1802 900	Request for expedited examination of a design application	

Other fee (specify)

\*Reduced by Basic Filing Fee Paid

**SUBTOTAL (3)** (\$ ) 0.00**SUBMITTED BY**

Name (Print/Type) Sara D Vinarov

Registration No. 48,524  
(Attorney/Agent)

(Complete if applicable)

Telephone 608/251-5000

Signature

Date April 9, 2004

**WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

374593

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.





FILED WITH APPLICATION  
NO. 09/643,189

I hereby certify that this correspondence is being deposited with the United States Postal Services on the date set forth below as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Date of Signature

and Deposit:

June 19, 1998

Jan C. Baker

Attorney of Record

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Divisional Application Of:

Applicants: Rui Sousa, et al.  
Serial No.: 08/713,331  
Filed: September 13, 1996  
Title: METHODS FOR USING MUTANT RNA  
POLYMERASES WITH REDUCED  
DISCRIMINATION BETWEEN NON-CANONICAL  
AND CANONICAL NUCLEOSIDE  
TRIPHOSPHATES  
Art Unit: 1809  
Examiner: A. Nelson

Assistant Commissioner for Patents  
Washington, D.C. 20231

---

INFORMATION DISCLOSURE STATEMENT

---

Dear Sir: -

Pursuant to 37 C.F.R. 1.98, Applicants in the above-identified patent application wish to bring to the attention of the Examiner for consideration in connection with the examination on the merits of this patent application. As this information duplicates information presented in related case Serial No. 08/713,331, Applicants have not provided copies of the documents.

U.S. Patents

Mullis, et al.; 4,683,195; July 28, 1987.

#### Other Document

"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," Biotechniques 9(2):142-146, 1990.

W.M. Barnes, "DNA Sequencing by Partial Ribosubstitution," J. Mol. Biol. 119:83-99, 1978.

E.T. Butler and M.J. Chamberlin, "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5772-5778, 1982.

C. Cazenave, et al., "RNA template-directed RNA synthesis by T7 RNA polymerase," PNAS 91:6972-6976, 1994.

D.H. Jones and B.H. Howard, "A Rapid Method for Recombination and Site-Specific Mutagenesis by Placing Homologous Ends on DNA Using Polymerase Chain Reaction," Biotechniques 10(1):62-66, 1991.

G.A. Kassavetis, et al., "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5779-5788, 1982.

D.A. Kostyuk, et al., "Mutants of T7 RNA polymerase that are able to synthesize both RNA and DNA," FEBS Letters 369:165-168, 1995.

H. Kotani, et al., "Nucleotide sequence and expression of the cloned gene of bacteriophage SP6 RNA polymerase," Nucl. Acids Res. 15(6):2653-2664, 1987.

R. Sousa and R. Padilla, "A mutant T7 RNA polymerase as a DNA polymerase," EMBO J. 14(18):4609-4621, 1995.

E. Uhlmann, et al., "Antisense oligonucleotides: A new therapeutic principle," Chem. Rev. 90:543-593, 1990.

A. Wolfgang, et al., "Kinetic characterization of ribonuclease-resistant 2'-modified hammerhead ribozymes," Science 253:314-317, 1991.

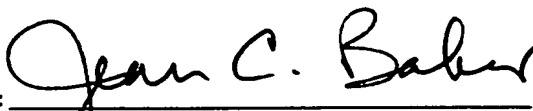
No fees are believed necessary to enter this statement. However, if any fees are necessary please charge Deposit Account 17-0055.

Respectfully submitted,

Rui Sousa, et al.

June 19, 1998

By:

  
Jean C. Baker  
QUARLES & BRADY  
411 East Wisconsin Avenue  
Milwaukee, WI 53202  
Reg. No.: 35,433  
(414) 277-5709

Sheet 1 of 2Form PTO-1449  
(Rev. 2-88)U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
310307.90061APPLICATION NO.  
Divisional of  
08/713,331INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT

(Use several sheets if necessary)

APPLICANT  
Rui Sousa, et al.FILING DATE  
September 13, 1996GROUP  
1809

## U.S. PATENT DOCUMENTS

EXAMINER'S INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	4,683,195	07/28/87	Mullis, <u>et al.</u>			

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

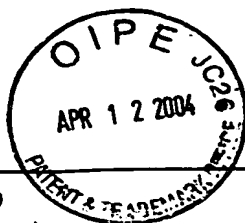
## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," <u>Biotechniques</u> 9(2):142-146, 1990.
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		G.A. Kassavetis, <u>et al.</u> , "Bacteriophage SP6-specific RNA Polymerase," <u>J. Biol. Chem.</u> 257(10):5779-5788, 1982.

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if a citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Sheet 2 of 2Form PTO-1449  
(Rev. 2-88)U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
310307.90061APPLICATION NO.  
Divisional of  
08/713,331INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT

(Use several sheets if necessary)

APPLICANT  
Rui Sousa, et al.FILING DATE  
September 13, 1996GROUP  
1809

## U.S. PATENT DOCUMENTS

EXAMINER'S INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		D.A. Kostyuk, <u>et al.</u> , "Mutants of T7 RNA polymerase that are able to synthesize both RNA and DNA," <u>FEBS Letters</u> 369:165-168, 1995.
		H. Kotani, <u>et al.</u> , "Nucleotide sequence and expression of the cloned gene of bacteriophage SP6 RNA polymerase," <u>Nucl. Acids Res.</u> 15(6):2653-2664, 1987.
		R. Sousa and R. Padilla, "A mutant T7 RNA polymerase as a DNA polymerase," <u>EMBO J.</u> 14(18):4609-4621, 1995.
		E. Uhlmann, <u>et al.</u> , "Antisense oligonucleotides: A new therapeutic principle," <u>Chem. Rev.</u> 90:543-593, 1990.
		A. Wolfgang, <u>et al.</u> , "Kinetic characterization of ribonuclease-resistant 2'-modified hammerhead ribozymes," <u>Science</u> 253:314-317, 1991.

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if a citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



EXPRESS MAIL LABEL NO. EL743811362US

FILED WITH APPLICATION  
NO. 09/965,346

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Rui Sousa, et al.  
Serial No.: --  
Filed: Herewith  
Title: METHODS FOR USING MUTANT RNA POLYMERASES WITH  
REDUCED DISCRIMINATION BETWEEN NON-CANONICAL  
AND CANONICAL NUCLEOSIDE TRIPHOSPHATES  
Art Unit: --  
Examiner: --  
Attorney Docket: 310307.90061

Commissioner for Patents  
Washington, D.C. 20231

**INFORMATION DISCLOSURE STATEMENT**

Dear Sir:

Pursuant to 37 C.F.R. 1.98, Applicants in the above-identified patent application wish to bring to the attention of the Examiner the information listed on the enclosed Form PTO-1449 for consideration in connection with the examination on the merits of this patent application. As this information was either previously submitted to, or cited by, the Office, in related cases Serial Nos. 08/713,331 and 09/643,189, Applicants have not provided copies of the documents.

U.S. Patents

Mullis, et al.; 4,683,195; July 28, 1987.

Other Documents

"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides,"  
Biotechniques 9(2):142-146, 1990.

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E.T. Butler and M.J. Chamberlin, "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5772-5778, 1982.

C. Cazenave, et al., "RNA template-directed RNA synthesis by T7 RNA polymerase," PNAS 91:6972-6976, 1994.

D.H. Jones and B.H. Howard, "A Rapid Method for Recombination and Site-Specific Mutagenesis by Placing Homologous Ends on DNA Using Polymerase Chain Reaction," Biotechniques 10(1):62-66, 1991.

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D.A. Kostyuk, et al., "Mutants of T7 RNA polymerase that are able to synthesize both RNA and DNA," FEBS Letters 369:165-168, 1995.

H. Kotani, et al., "Nucleotide sequence and expression of the cloned gene of bacteriophage SP6 RNA polymerase," Nucl. Acids Res. 15(6):2653-2664, 1987.

R. Sousa and R. Padilla, "A mutant T7 RNA polymerase as a DNA polymerase," EMBO J. 14(18):4609-4621, 1995.

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Kostyuk et al., "Mutants of T7 RNA polymerase that are able to synthesize both RNA and DNA", FEBS Letters, Vol. 369, pages 165-168, 1995.

Sousa et al., "A mutant T7 RNA polymerase as a DNA polymerase", The EMBO Journal, Vol. 14, No. 18, pages 4609-4621, 1995.

No fees are believed necessary to enter this statement. However, if any fees are necessary please charge Deposit Account 17-0055.

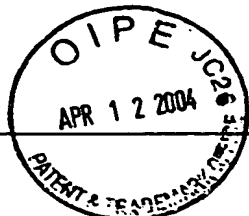
Respectfully submitted,

Rui Sousa, et al.

September 27, 2001

By: \_\_\_\_\_  
Jean C. Baker  
QUARLES & BRADY LLP  
411 East Wisconsin Avenue  
Milwaukee, WI 53202  
Reg. No.: 35,433  
(414) 277-5709



Sheet 1 of 2Form PTO-1449  
(Rev. 2-88)U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
310307.90061APPLICATION NO.  
Divisional of  
08/713,331INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT

(Use several sheets if necessary)

APPLICANT  
Rui Sousa, et al.FILING DATE  
September 13, 1996GROUP  
1809

## U.S. PATENT DOCUMENTS

EXAMINER'S INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	4,683,195	07/28/87	Mullis, <u>et al.</u>			

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

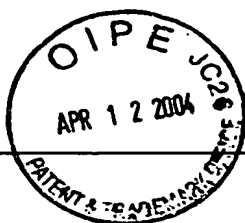
## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," <u>Biotechniques</u> 9(2):142-146, 1990.
		W.M. Barnes, "DNA Sequencing by Partial Ribosubstitution," <u>J. Mol. Biol.</u> 119:83-99, 1978.
		E.T. Butler and M.J. Chamberlin, "Bacteriophage SP6-specific RNA Polymerase," <u>J. Biol. Chem.</u> 257(10):5772-5778, 1982.
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		D.H. Jones and B.H. Howard, "A Rapid Method for Recombination and Site-Specific Mutagenesis by Placing Homologous Ends on DNA Using Polymerase Chain Reaction," <u>Biotechniques</u> 10(1):62-66, 1991.
		G.A. Kassavetis, <u>et al.</u> , "Bacteriophage SP6-specific RNA Polymerase," <u>J. Biol. Chem.</u> 257(10):5779-5788, 1982.

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if a citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



Form PTO-1449  
(Rev. 2-88)

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO.  
310307.90061

APPLICATION NO.  
Divisional of  
08/713,331

**INFORMATION DISCLOSURE STATEMENT  
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Rui Sousa, et al.

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		A. Wolfgang, <u>et al.</u> , "Kinetic characterization of ribonuclease-resistant 2'-modified hammerhead ribozymes," <u>Science</u> 253:314-317, 1991.

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EXPRESS MAIL LABEL NO. EJ636887252US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Continuation Of:

Applicants: Rui Sousa, et al.  
Serial No.: 09/100,803  
Filed: June 19, 1998  
Title: METHODS FOR USING MUTANT RNA  
POLYMERASES WITH REDUCED  
DISCRIMINATION BETWEEN NON-CANONICAL  
AND CANONICAL NUCLEOSIDE  
TRIPHOSPHATES  
Art Unit: 1655  
Examiner: A. Chakrabarti

Commissioner for Patents  
Washington, D.C. 20231

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INFORMATION DISCLOSURE STATEMENT

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Dear Sir:

Pursuant to 37 C.F.R. 1.98, Applicants in the above-identified patent application wish to bring to the attention of the Examiner for consideration in connection with the examination on the merits of this patent application. As this information duplicates information presented in related case Serial No. 08/713,331, Applicants have not provided copies of the documents.

U.S. Patents

Mullis, et al.; 4,683,195; July 28, 1987.

### Other Document

"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," Biotechniques 9(2):142-146, 1990.

W.M. Barnes, "DNA Sequencing by Partial Ribosubstitution," J. Mol. Biol. 119:83-99, 1978.

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A. Wolfgang, et al., "Kinetic characterization of ribonuclease-resistant 2'-modified hammerhead ribozymes," Science 253:314-317, 1991.

No fees are believed necessary to enter this statement. However, if any fees are necessary please charge Deposit Account 17-0055.

Respectfully submitted,

Rui Sousa, et al.

August 21, 2000

By: \_\_\_\_\_  
Jean C. Baker  
QUARLES & BRADY LLP  
411 East Wisconsin Avenue  
Milwaukee, WI 53202  
Reg. No.: 35,433  
(414) 277-5709

Sheet 1 of 2Form PTO-1449  
(Rev. 2-88)U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
310307.90061

APPLICATION NO.

INFORMATION DISCLOSURE STATEMENT  
BY APPLICANTAPPLICANT  
Rui Sousa, et al.

FILING DATE

GROUP

(Use several sheets if necessary)

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						YES	NO

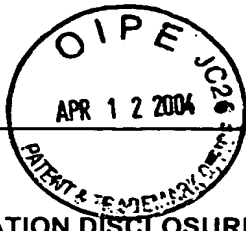
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		D.H. Jones and B.H. Howard, "A Rapid Method for Recombination and Site-Specific Mutagenesis by Placing Homologous Ends on DNA Using Polymerase Chain Reaction," <u>Biotechniques</u> 10(1):62-66, 1991.
		G.A. Kassavetis, <u>et al.</u> , "Bacteriophage SP6-specific RNA Polymerase," <u>J. Biol. Chem.</u> 257(10):5779-5788, 1982.

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Sheet 2 of 2

Form PTO-1449  
(Rev. 2-88)U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
310307.90061

APPLICATION NO.

INFORMATION DISCLOSURE STATEMENT  
BY APPLICANTAPPLICANT  
Rui Sousa, et al.

FILING DATE

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Date of Signature

and Deposit: \_\_\_\_\_

\_\_\_\_\_  
Attorney of Record

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Rui Sousa, et al.  
Serial No.: 08/713,331  
Filed: September 13, 1996  
Title: METHODS FOR USING MUTANT RNA  
POLYMERASES WITH REDUCED  
DISCRIMINATION BETWEEN NON-CANONICAL  
AND CANONICAL NUCLEOSIDE  
TRIPHOSPHATES  
Art Unit: 1809  
Examiner: A. Nelson

Assistant Commissioner for Patents  
Washington, D.C. 20231

---

**INFORMATION DISCLOSURE STATEMENT**

---

Dear Sir:

Pursuant to 37 C.F.R. 1.98, enclosed herewith are documents which the Applicants in the above-identified patent application wish to bring to the attention of the Examiner for consideration in connection with the examination on the merits of this patent application.

Other Document

"Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," Biotechniques 9(2):142-146, 1990.

W.M. Barnes, "DNA Sequencing by Partial Ribosubstitution," J. Mol. Biol. 119:83-99, 1978.



E.T. Butler and M.J. Chamberlin, "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5772-5778, 1982.

D.H. Jones and B.H. Howard, "A Rapid Method for Recombination and Site-Specific Mutagenesis by Placing Homologous Ends on DNA Using Polymerase Chain Reaction," Biotechniques 10(1):62-66, 1991.

G.A. Kassavetis, et al., "Bacteriophage SP6-specific RNA Polymerase," J. Biol. Chem. 257(10):5779-5788, 1982.

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R. Sousa and R. Padilla, "A mutant T7 RNA polymerase as a DNA polymerase," EMBO J. 14(18):4609-4621, 1995.

The enclosed Fee Transmittal directs any fees that are deemed necessary to be charged to deposit account 17-0055.

Respectfully submitted,

Rui Sousa, et al.

August 28, 1997

By: \_\_\_\_\_  
Jean C. Baker  
QUARLES & BRADY  
411 East Wisconsin Avenue  
Milwaukee, WI 53202  
Reg. No.: 35,433  
(414) 277-5709



EXAMINER	DATE CONSIDERED
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**(Use as many sheets as necessary)**

Sheet	1	of	3
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Application Number	10/689,495
Filing Date	10/20/2003
First Named Inventor	Rui Sousa
Art Unit	
Examiner Name	
Attorney Docket Number	310307.90240

[illegible]

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)	MM-DD-YYYY			
		EP 0 655 506 B1	05/31/1995	Tabor et al.		

Examiner Signature		Date Considered	
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This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		<b>Complete if Known</b>			
		Application Number	10/689,495		
		Filing Date	10/20/2003		
		First Named Inventor	Rui Sousa		
		Art Unit			
		Examiner Name			
Sheet	2	of	3	Attorney Docket Number	310307.90240

OTHER PRIOR ART—NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Bonner, et al., "Mutations in T7 RNA polymerase that support the proposal for a common polymerase active site structure," The EMBO Journal 11:3767-3775 (1992)	
		Bonner et al., "Characterization of a Set of T7 RNA Polymerase Active Site Mutants," The Journal of Biological Chemistry 269:25120-25128 (1994)	
		Briebe, et al., "Role of T7 Polymerase His784 in Start Site Selection and Initial Transcription," Biochemistry 41:5144-5149 (2002)	
		Cheetham et al., "Structure of a Transcribing T7 RNA Polymerase Initiation Complex," Science 286:2305-2309 (1999)	
		Cunningham et al, "Use of Inorganic Pyrophosphatase to Improve the Yield of In Vitro Transcription Reactions Catalyzed by T7 RNA Polymerase," BioTechniques 9:713-714 (1990)	
		Delarue, et al., "An attempt to unify the structure of polymerases," Protein Engineering 3:461-467 (1990)	
		Huang et al., "Mechanism of Ribose 2'-Group Discrimination by an RNA Polymerase," Biochemistry 36:8231-8242 (1997)	
		Huang et al., "Misincorporation by Wild-Type and Mutant T7 RNA Polymerases: Identification of Interactions that Reduce Misincorporation Rates by Stabilizing the Catalytically Incompetent Open Conformation," Biochemistry 39:11571-11580 (2000)	
		Makarova et al., "Transcribing of Escherichia coli genes with mutant T7 RNA polymerases: Stability of lacZ mRNA inversely correlates with polymerase speed," Proc. Natl. Acad. Sci. USA 92:12250-12254 (1995)	
		Mentesana et al., "Characterization of Halted T7 RNA Polymerase Elongation Complexes Reveals Multiple Factors that Contribute to Stability," J. Mol. Biol. 302:1049-1062 (2000)	

Examiner Signature		Date Considered	
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

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Approved for use through 10/31/2002. OMB 0651-0031

U. S. Patent and Trademark Office: U. S. DEPARTMENT OF COMMERCE

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Substitute for form 1449B/PTO		<b>Complete if Known</b>	
		Application Number	10/689,495
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Filing Date	10/20/2003
		First Named Inventor	Rui Sousa
		Group Art Unit	
		Examiner Name	
		Attorney Docket Number	310307.90240
Sheet	3	of	3

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Moroney et al., "Abortive Products as Initiating Nucleotides during Transcription by T7 RNA Polymerase," Biochemistry 30:10343-10349 (1991)	
		Osumi-Davis et al., "Bacteriophage T7 RNA Polymerase and Its Active-site Mutants," J. Mol. Biol. 237:5-19 (1994)	
		Padilla et al., "Efficient Synthesis of nucleic acids heavily modified with non-canonical ribose 2'-groups using a mutant T7 RNA polymerase (RNAP)," Nucleic Acids Research 27:1561-1563 (1999)	
		Padilla et al., "A Y639F/H784A T7 RNA polymerase double mutant displays superior properties for synthesizing RNAs with non-canonical NTPs," Nucleic Acids Research 30:e138 (2002)	
		Patra et al., "Isolation and Characterization of Mutant Bacteriophage T7 RNA Polymerases," J. Mol. Biol. 224:307-318 (1992)	
		Tabor et al., "A Bacteriophage T7 RNA Polymerase/Promoter System for Controlled Exclusive Expression of Specific Genes," Proc. Natl. Acad. Sci. USA 82:1074-1078 (1985)	
		Tabor et al., "Effect of manganese ions on the incorporation of dideoxynucleotides by bacteriophage T7 DNA polymerase and Escherichia coli DNA polymerase I," Proc. Natl. Acad. Sci. USA 86:4076-4080 (1989)	
		Zhang et al., "Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution," PNAS 98:5497-5502 (2001)	

Examiner Signature		Date Considered	
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<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

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